Tissue-engineered small intestine and stomach form from autologous tissue in a preclinical large animal model.

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Authors: Frederic G Sala, Shaun M Kunisaki, Erin R Ochoa, Joseph Vacanti, Tracy C Grikscheit

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Public Summary:

Scientific Abstract:
BACKGROUND: Tissue-engineered small intestine, stomach, large intestine, esophagus, and gastroesophageal (GE) junction have been successfully formed from syngeneic cells, and employed as a rescue therapy in a small animal model. The purpose of this study is to determine if engineered intestine and stomach could be generated in an autologous, preclinical large animal model, and to identify if the tissue-engineered intestine retained features of an intact stem cell niche. METHODS: A short segment of jejunum or stomach was resected from 6-wk-old Yorkshire swine. Organoid units, multicellular clusters with predominantly epithelial content, were generated and loaded onto biodegradable scaffold tubes. The constructs were then implanted intraperitoneally in the autologous host. Seven wk later, all implants were harvested and analyzed using histology and immunohistochemistry techniques. RESULTS: Autologous engineered small intestine and stomach formed. Tissue-engineered intestinal architecture replicated that of native intestine. Histology revealed tissue-engineered small intestinal mucosa composed of a columnar epithelium with all differentiated intestinal cell types adjacent to an innervated muscularis mucosae. Intestinal subepithelial myofibroblasts, specialized cells that participate in the stem cell niche formation, were identified. Moreover, cells positive for the putative intestinal stem cell marker, doublecortin and CaM kinase-like-1 (DCAMKL-1) expression were identified at the base of the crypts. Finally, tissue-engineered stomach also formed with antral-type mucosa (mucus cells and surface foveolar cells) and a muscularis. CONCLUSION: We successfully generated tissue-engineered intestine with correct architecture, including features of an intact stem cell niche, in the pig model. To our knowledge, this is the first demonstration in which tissue-engineered intestine was successfully generated in an autologous manner in an animal model, which may better emulate a human host and the intended therapeutic pathway for humans.